

## REMARKS

Claims 25-65 are pending, with claims 51, 52 and 57-65 having been withdrawn from further consideration. By the present communication, Applicants have canceled claims 28-30, 36-39, 41, 42, 53 and 54 without prejudice, added new claims 66-75, and amended claims 25, 26, 34, 35, 43 and 44 to define Applicants' invention with greater particularity. The amendments do not raise any issues of new matter and the amended claims do not present new issues requiring further consideration or search. Support for the new claims may be found, among others, in Examples 3-5 of the specification as filed. Accordingly, upon entry of this communication, claims 25-27, 31-35, 40, 43-50, 55, 56 and 66-75 will be under consideration.

### Priority

Applicants traverse the accord of priority of the present application to November 10, 1997. Specifically, the Examiner alleges that the parent applications do not disclose any variants (mutants) which are responsible for increased muscle mass in non-human subjects. Applicants submit that the priority documents fully support claims directed to a method for detecting the presence of a target myostatin variant nucleic acid sequence in a nucleic acid-containing specimen wherein the specimen is from a subject having increased muscle mass or having a predisposition for increased muscle mass as compared to a subject having a wild-type nucleic acid sequence. For example, issued U.S. Pat. No. 5,994,618, to which this application claims priority, is directed to myostatin knock-out transgenic animals, which have increased muscle mass as compared to a subject having a wild-type nucleic acid sequence. The Examples of that patent, including Example 8, as well as issued claims 2 and 5, provide support for the methods for detecting variant myostatin in a sample, whether in one or both alleles. Further, the priority applications provide support for the importance of the mature or C-terminal region of the myostatin polypeptide, where exon 3 and the specific 11 base-pair mutation are found. Finally, Applicants were the first to clone the bovine myostatin sequence, which is provided in the priority applications as well and deposited in GenBank as accession no. AF019620. Accordingly, accord of the benefit of priority to at least as early as October 26, 1995 is respectfully requested.

**Objection to the Claims**

Applicants respectfully traverse the objection to claims 34, 35, 43 and 44 for allegedly reciting non-elected inventions (SEQ ID NOs). Applicants further traverse the objection to claim 25 as allegedly containing a typographical error. However, in order to further prosecution and reduce the issues, Applicants have amended claims 25, 34, 35, 43 and 44 to correct the typographical error and to cancel non-elected subject matter without prejudice. Accordingly, withdrawal of the objection is respectfully requested.

**Objection to the Specification**

Applicants respectfully traverse the objection to the specification as allegedly failing to comply with the Sequence Requirements as set forth in 37 CFR 1.821-1.825. However, in order to further prosecution and reduce the issues, Applicants have amended the paragraph beginning on page 4, line 7 of the Specification, to include the appropriate sequence identifiers. Accordingly, withdrawal of the objection is respectfully requested.

**Rejection under 35 U.S.C. §112, Second Paragraph**

Applicants respectfully traverse the rejection of claims 25-28, 31-37, 41, 42 and 54-56 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner alleges that claim 25 is indefinite because it is unclear whether "a subject" is limited to a non-human subject, or if the term embraces human subjects as well. Claims 26-28, 31-37, 41, 42 and 54-56 are also allegedly indefinite for depending upon claim 25. In order to further prosecution and reduce the issues, Applicants have amended claim 25 to indicate that the subject is bovine.

The Examiner further alleges that claim 26 is indefinite because it is unclear which nucleic acid is being amplified. In order to further prosecution and reduce the issues, Applicants have amended claim 26 to indicate that the variant target nucleic acid is being amplified.

Finally, the Examiner alleges that claim 28 is indefinite because of a typographical error in the accession number, and because referring to a nucleotide sequence only by its accession number is allegedly indefinite. Applicants respectfully note that the rejection should have

applied to claim 30 since claim 28 does not claim a sequence by accession number. While Applicants have canceled claim 30 without prejudice, Applicants respectfully submit that the identification of the sequence by GenBank Accession number is acceptable under M.P.E.P. §2173.05(t), which reads, in part, "Chemical compounds may be claimed by a name that adequately describes the material to one skilled in the art." The Examiner alleges the nucleotide sequences found in GenBank constantly go through sequence revisions. However, no evidence is provided to support the Examiner's assertion. Applicants submit that GenBank Accession No. AF019620 was deposited on November 21, 1997, and remains listed as version AF019620.1 (see [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=nucleotide&dopt=GenBank&list\\_uids=2623567](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=nucleotide&dopt=GenBank&list_uids=2623567)), a copy of which is attached as Exhibit A. Accordingly, Applicants respectfully submit that the rejection of claim 30 is moot.

Accordingly, for the reasons provided above, Applicants respectfully request withdrawal of the rejection of claims 25-28, 31-37, 41, 42 and 54-56 under 35 U.S.C. §112, second paragraph.

**Rejection under 35 U.S.C. §112, First Paragraph**

Applicants respectfully traverse the rejection of claims 25-42 and 54-56 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention at the time the application was filed. Specifically, the Examiner alleges that the specification does not reasonably provide enablement for a method for detecting the presence of a target myostatin variant nucleic acid sequence in a nucleic acid specimen, wherein the specimen is avian, ovine, piscine, baboon, murine, or picine, wherein the target myostatin variant nucleotide is any variant myostatin sequence, and wherein the variant sequence is found in only one allele. Applicants have canceled claims 28-30, 36-39, 41, 42 and 54, rendering the rejection moot as to those claims. Further, in order to reduce the issues and further prosecution, Applicants have amended claim 25 to limit the claims to detecting the presence of a variant Piedmontese myostatin having a homozygous G1056A substitution. Accordingly, withdrawal of the rejection is respectfully requested.

**Rejection under 35 U.S.C. §102**

Applicants respectfully traverse the rejection of claims 25-30, 33, 36, 37, 40, 42 and 54-56 under 35 U.S.C. §102(a) as allegedly being anticipated by Kambadur et al. (Genome Research September 1997, vol. 7, no. 9, pages 910-916) (hereinafter “Kambadur”). Applicants have canceled claims 28-30, 36, 37, 42 and 54, rendering the rejection moot as to those claims. Applicants submit herewith as Exhibit B, a Declaration under 37 C.F.R. § 1.131 with Exhibit 1, as filed during prosecution of U.S. Serial No. 08/967,089, now issued as U.S. Pat. No. 6,673,534, to which the present application has been accorded the benefit of priority. The Declaration demonstrates that the claimed invention was made in the United States prior to the September 1997 publication of Kambadur. Accordingly, it is submitted that Kambadur is not prior art with respect to the claimed invention. Withdrawal of the rejection is respectfully requested.

Applicants respectfully traverse the rejection of claims 25-29, 33, 36, 37, 40, 42 and 54-56 under 35 U.S.C. §102(e) as allegedly being anticipated by Grobet et al. (U.S. Pat. No. 6,103,466) (hereinafter “Grobet”). Applicants have canceled claims 28, 29, 36, 37, 42 and 54, rendering the rejection moot as to those claims. However, Applicants submit that Grobet is not available as prior art since Applicants claim priority to patent applications dating back to October 26, 1995, over two years before the Grobet priority date. Applicants submit that the priority documents fully support claims directed to a method for detecting the presence of a target myostatin variant nucleic acid sequence in a nucleic acid-containing specimen wherein the specimen is from a subject having increased muscle mass or having a predisposition for increased muscle mass as compared to a subject having a wild-type nucleic acid sequence. For example, issued U.S. Pat. No. 5,994,618, to which this application claims priority, is directed to myostatin knock-out transgenic animals, which have increased muscle mass as compared to a subject having a wild-type nucleic acid sequence. The Examples of that patent, including Example 8, as well as issued claims 2 and 5, provide support for the methods for detecting variant myostatin in a sample, whether in one or both alleles. Further, the priority applications provide support for the importance of the mature or C-terminal region of the myostatin polypeptide, where exon 3 and the specific 11 base-pair mutation are found. Finally, Applicants were the first to clone the bovine myostatin sequence, which is provided in the priority

applications as well and deposited in GenBank as accession no. AF019620. Accordingly, Applicants submit that Grobet is not prior art and that the claims are fully supported by the priority documents, dating back at least to October 26, 1995, and therefore request that the rejection be withdrawn.

**Rejection under 35 U.S.C. §103**

Applicants respectfully traverse the rejection of claims 34, 35 and 43-46 under 35 U.S.C. §103(a) as allegedly being unpatentable over Grobet. Specifically, the Examiner alleges that Grobet teaches a method of detecting the presence of a an 11-base pair deletion in a myostatin gene from a subject wherein the presence of the mutation is correlated with the subject having an increased muscle mass. As discussed above, Applicants submit that Grobet is not available as prior art since Applicants claim priority to patent applications dating back to October 26, 1995, over two years before the Grobet priority date. Applicants submit that the priority applications provide support for the importance of the mature or C-terminal region of the myostatin polypeptide, where exon 3 and the specific 11 base-pair mutation are found. Applicants, and not Grobet, had first identified and disclosed this important region of the gene and polypeptide, and therefore it was Applicants' findings that led to the development of primers and probes specifically directed toward this region of myostatin. Furthermore, in the absence of Applicants' teachings as far back at least as October 26, 1995, there would have been no motivation to produce kits containing specific primers to amplify exon 3 of myostatin, since Applicants determined the importance of the mature, active region of myostatin, which includes specifically, exon 3. Thus, Applicants submit that not only is Grobet not available as prior art, but the teaching in Grobet could not render the present invention obvious. Accordingly, withdrawal of the rejection is respectfully requested.

Applicants respectfully traverse the rejection of claims 31, 32, 34, 35, 43-50 and 53 under 35 U.S.C. §103(a) as allegedly being unpatentable over Kambadur in view of Valent et al. (Molecular Microbiology, July 1997, vol. 25, no. 1, pages 53-64) (hereinafter "Valent"). Applicants have canceled claim 53, rendering the rejection moot as to that claim. As discussed above, Applicants submit herewith a Declaration under 37 C.F.R. § 1.131, with Exhibit 1, as

In re Application of:  
Lee and McPherron  
Application No.: 10/662,003  
Filed: September 11, 2003  
Page 15

PATENT  
Attorney Docket No.: JHU1410-1

filed during prosecution of U.S. Serial No. 08/967,089, now issued as U.S. Pat. No. 6,673,534, to which the present application has been accorded the benefit of priority. The Declaration demonstrates that the claimed invention was made in the United States prior to the September 1997 publication of Kambadur. Accordingly, it is submitted that Kambadur is not prior art with respect to the claimed invention. Since Valent does not teach or suggest the claimed invention, withdrawal of the rejection is respectfully requested.

In re Application of:  
Lee and McPherron  
Application No.: 10/662,003  
Filed: September 11, 2003  
Page 16

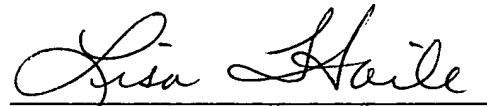
PATENT  
Attorney Docket No.: JHU1410-1

**CONCLUSION**

In light of the Amendments and Remarks herein, Applicant submits that the claims are in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, he is invited to call the undersigned attorney.

Enclosed is Check No. 582463 in the amount of \$225.00 for the two-month Petition for Extension of Time fee. No other fee is deemed necessary with the filing of this paper. However, if any other fee is required, authorization is hereby given to the Commissioner to charge the amount of any such fee, or credit any overpayment, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A copy of the Transmittal Sheet is enclosed.

Respectfully submitted,



Lisa A. Haile, J.D., Ph.D.  
Registration No. 38,347  
Telephone: (858) 677-1456  
Facsimile: (858) 677-1465

Date: June 30, 2006

DLA PIPER RUDNICK GRAY CARY US LLP  
4365 Executive Drive, Suite 1100  
San Diego, California 92121-2133  
USPTO CUSTOMER NO. 28213

NCBI Nucleotide [Sign In] [Register]

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Books

Search Nucleotide for  Go Clear

Limits Preview/Index History Clipboard Details

Display GenBank Show 20 Send to

Range: from begin to end  Reverse complemented strand Features: + Refresh

1: AF019620. Reports Bos taurus myosta...[gi:2623567]

Links

Features Sequence

LOCUS AF019620 1128 bp mRNA linear MAM 21-NOV-1997  
 DEFINITION Bos taurus myostatin (MSTN) mRNA, complete cds.  
 ACCESSION AF019620  
 VERSION AF019620.1 GI:2623567  
 KEYWORDS  
 SOURCE Bos taurus (cattle)  
 ORGANISM Bos taurus  
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae; Bovinae; Bos.  
 REFERENCE 1 (bases 1 to 1128)  
 AUTHORS McPherron, A.C. and Lee, S.J.  
 TITLE Double muscling in cattle due to mutations in the myostatin gene  
 JOURNAL Proc. Natl. Acad. Sci. U.S.A. 94 (23), 12457-12461 (1997)  
 PUBMED 9356471  
 REFERENCE 2 (bases 1 to 1128)  
 AUTHORS McPherron, A.C. and Lee, S.J.  
 TITLE Direct Submission  
 JOURNAL Submitted (15-AUG-1997) Molecular Biology and Genetics, Johns Hopkins University School of Medicine, 725 N. Wolfe St., Baltimore, MD 21205, USA  
 FEATURES Location/Qualifiers  
 source 1..1128  
 /organism="Bos taurus"  
 /mol\_type="mRNA"  
 /db\_xref="taxon:9913"  
 /tissue\_type="skeletal muscle"  
 gene 1..1128  
 /gene="MSTN"  
 CDS 1..1128  
 /gene="MSTN"  
 /note="transforming growth factor-beta superfamily member; growth/differentiation factor-8; GDF-8"  
 /codon\_start=1  
 /product="myostatin"  
 /protein\_id="AAB86687.1"  
 /db\_xref="GI:2623568"  
 /translation="MQKLQISVYIYLFMLIVAGPVDLNENSEQKENVEKEGLCNACLW  
 RENTTSSRLEAIKIQILSKLRLTAPNISKDAIRQLLPKAPPLELIDQFDVQRDASS  
 DGSLEDDDYHARTEVITMPTESDLTQVEGKPCKCFKFSSKIQYNKLVKAQLWIYL  
 RPVKTPATVFVQILRLIKPMKDGTTRYTGIRSLKLDMNPGTGIWQSIDVKTVLQNWLKQ  
 PESNLGIEIKALDENGHDLAVTFPEPGEDGLTPFLEVKTDTPKRSRRDFGLDCDEHS  
 TESRCCRYPLTVDFEAFGWDWIIAPKRYKANYCSGECEFVFLQKYPTHTLHQANPRG

SAGPCCTPTKMSPINMLYFNNEGQIIFYGKIPAMVVDRCGCS"

## ORIGIN

1 atgcaaaaac tgcaaattc tggatattt tacctattt tgctgattt tgctggccca  
61 gtggatctga atgagaacag cgagcagaag gaaaatgtgg aaaaagaggg gctgtgtatc  
121 gcatgtttgt ggaggaaaaa cactacatcc tcaagactag aagccataaa aatccaaatc  
181 ctcagtaaac ttgccttgg aacagctcct aacatcagca aagatgttat cagacaactt  
241 ttgcccagg ctcctccact ctttggactt attgtatcgt tgcgtgttccaa gagagatgcc  
301 agcagtgacg gtccttgg aagacgttac taccacgcca ggacggaaac ggtcattacc  
361 atgcccacgg agtctgtatc tctaacgcaa gtggaaaggaa aacccaaatg ttgcttctt  
421 aaatttagct ctaagataca atacaataaa cttttttttt cccaaactgtt gatatatctg  
481 aggccctgtca agactcctgc gacagtgttt gtgcattttcc ttagactcat cttttttttt  
541 aaagacggta caaggtatac tggatccga tctctgaaac ttgacatgaa cccaggcact  
601 ggtatttggc agagcatttga tttttttttt gttttttttt gttttttttt gttttttttt  
661 tccaaacttag gcattttttt cttttttttt gatgataatg gccatgtatc tgctgttacc  
721 ttcccaacttgc cttttttttt gttttttttt gttttttttt gttttttttt gttttttttt  
781 cttttttttt gttttttttt gttttttttt gttttttttt gttttttttt gttttttttt  
841 tgctgtcggtt accctcttac tttttttttt gttttttttt gttttttttt gttttttttt  
901 cttttttttt gttttttttt gttttttttt gttttttttt gttttttttt gttttttttt  
961 tttttttttt gttttttttt gttttttttt gttttttttt gttttttttt gttttttttt  
1021 tttttttttt gttttttttt gttttttttt gttttttttt gttttttttt gttttttttt  
1081 tacggaaaga ttccagccat ggtttttttt gttttttttt gttttttttt gttttttttt

//

[Disclaimer](#) | [Write to the Help Desk](#)  
[NCBI](#) | [NLM](#) | [NIH](#)

Apr 11 2006 19:57:30